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Dr. Michael Shelby, Director
CERHR, NIEHS
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PROPYLENE GLYCOLS TOXICITY

Dear Dr. Shelby:

The March issue of the NTP Update mentioned on p.6 that future evaluation of ethylene glycol and the propylene glycols was planned and asked for comments and info. It did not say whether you wanted information on 1, 2 – propylene glycol or 1, 3-propylene glycol, or both. I have a few comments about the 1,2 isomer that I feel you should consider, if you haven't already considered them.

The 1,2 isomer is an asymmetric molecule, since it has no center, or axis, or plane of symmetry because of the four different substituents on the #2 carbon. Therefore, it can exist in two stereoisomeric forms, which, if like many other individual stereoisomers of a stereoisomer pair, can have dramatically different toxicities. One can be relatively toxic, while the other is relatively benign. This phenomenon is seen and recognized in the pharmaceutical industry where it often is seen that one stereoisomer has most of the activity and the other is essentially inactive.

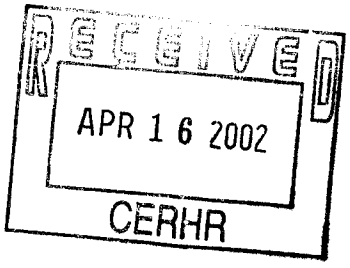
The usual industrial processes which generate asymmetric molecules, generate a nearly 1:1 mixture of the two stereoisomers. As a result, the toxicity of the more toxic stereoisomer is diluted by ~half by the more benign stereoisomer. I don't know if the usual industrial process for producing 1,2-propylene glycol uses a stereospecific catalyst, but I doubt that it does. If it does not, the usual commercial product would contain nearly equal fractions of the two possible stereoisomers, which probably would have different levels of toxicity.

While we are cognizant of the level of toxicity of the current commercial 1,2-propylene glycol, if someone in the future finds a high value use for one of the stereoisomers, a process could be developed that would produce only one stereoisomer. If it is the more toxic stereoisomer, it will have lost the diluting effect of the less toxic stereoisomer and could have a totally unanticipated level of toxicity. (Of course, if the manufacturer got lucky, he could be producing only the less toxic stereoisomer.)

Therefore, I suggest that any toxicity program on 1,2-propylene glycol should recognize this asymmetry and its possible toxicity ramifications and should prepare sufficient amounts of the two stereoisomers to do at least minimal tox work on both, including mutagenicity studies.

Sincerely,

Richard S. Waritz, Ph.D., DABT, FATS



PropGlyToxNIEHS4_1102